UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/077,574	09/24/98	PANACCIO M	DAVIE60001AP

020995 HM12/0829
KNOBBE MARTENS OLSON & BEAR LLP
620 NEWPORT CENTER DRIVE
SIXTEENTH FLOOR
NEWPORT BEACH CA 92660

EXAMINER	
DEVI S	
ART UNIT	**PAPER NUMBER**
1645	16

DATE MAILED: 08/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/077,574	Panaccio et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 21, 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-36, 38, 39, 41-62, and 92-113* ~~is~~/are pending in the application.

4a) Of the above, claim(s) *3-5, 11, 13-31, 33-36, 40, 42, 44-62, 92, 93, 96-107 and 110-113* ~~is~~/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 6-10, 12, 32, 37-41, 43, 94, 95, 108, and 109* ~~is~~/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☒ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6.*
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 09/24/98 (paper no. 1), 08/03/00 (paper no. 9) and 05/21/01 (paper no. 14). With these, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election filed 05/21/01 (paper no. 14) of invention 2, claims 10, 12, 41 and 43, drawn to the polypeptide of SEQ ID NO: 2 and a method of using the same, in response to the lack of unity requirement mailed 12/18/00 (paper no. 13). Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

It is noted that Applicants have added new claims drawn to the elected polypeptide (SEQ ID NO: 2), a composition comprising the same, methods of using and making the same as well as claims drawn to the non-elected products: nucleic acid and host cell. Although the elected product of the invention and method of making and using the product is a permitted combination under PCT Rule 13.2, in the instant case, the special technical feature is already disclosed in the art. Labigne *et al.* (WO 9426901-A) disclose a polypeptide comprising an amino acid sequence having 67.2% (i.e., at least 40%) similarity to the claimed polypeptide. Therefore, the special technical feature is not a unifying feature. Technically, the absence of a special technical feature would permit the separation of a method of making the polypeptide and a method of using the polypeptide. Therefore, the elected claims 10, 12, 41 and 43, the linking claims 1, 2, 6-9, 32 and 37-40 and product-directed new claims 94, 95, 108 and 109 have been joined for purposes of examination.

Acknowledgment is made of Applicants' election of polypeptide species in claim 6; heat shock protein and flagellar basal body rod protein species in claims 9 and 40; and peptide, protein or polypeptide species in claim 37.

Status of Claims

3) Claims 63-76 and 78-90 have been canceled via the amendment filed 09/24/98.

Claims 1-32, 37, 40 and 77 have been amended via the amendment filed 09/24/98.

New claim 91 has been added via the amendment filed 09/24/98.

Claims 2-31, 33-62, 77, 91-93 have been amended via the amendment filed 08/03/00.

Claims 77 and 91 have been canceled via the amendment filed 21 May 2001.

Claims 10, 12, 41 and 43 have been amended via the amendment filed 21 May 2001.

New claims 94-113 have been added via the amendment filed 05/21/01.

Claims 1-36, 38, 39, 41-62 and 92-113 are pending.

Claims 1, 2, 6-10, 12, 32, 37-41 and 43, are drawn to non-elected product(s) and claims 3-5, 11, 13-31, 33-36, 42, 44-62, 92, 93, 96-107 and 110-113 have been withdrawn from consideration as being directed to non-elected inventions. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 10, 12, 41 and 43, drawn to a vaccine comprising polypeptide GroEL having SEQ ID NO: 2 and a method of using the same, have been elected and are under examination. Linking claims 1, 2, 6-9, 32 and 37-40, as related to an immunogenic component of *L. intracellularis* or a related microorganism and a method of using the product, have been joined with the elected claims. New claims 94, 95, 108 and 109, related to the elected product, presented via the amendment filed 05/21/01, have been joined with the elected claims.

An Action on the Merits for claims 1, 2, 6-10, 12, 32, 37-41, 43, 94, 95, 108 and 109, to the extent these claims encompass the polypeptide of SEQ ID NO: 2, is issued in the instant Office Action (paper no. 15).

Sequence Listing

4) Acknowledgment is made of Applicants' raw sequence listing which has been entered on 11/02/00 (paper no. 15).

Information Disclosure Statement

5) Acknowledgment is made of Applicants' Information Disclosure Statement filed

02/11/99 (paper no. 6). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 16).

Priority

6) This application is filed under 35 U.S.C. 371 of application PCT/AU96/00767, filed 11/29/96, which claims priority to applications, PB6910 and PN6911, both filed 11/30/95 in Australia. It is noted that a certified copy of application PB6910 is made of record.

Drawings

7) The drawings submitted 09/24/98 are not objected to by the Draftsperson under 37 C.F.R 1.84 or 1.152 and as such, the drawings have been approved as formal drawings.

Specification - Informalities

8) The specification is objected to for the following reason(s):

The use of the trademarks in the instant specification has been noted in this application. For example, see page 21, line 19: "XLI-Blue"; page 22, line 12 and page 24, line 27: "Tween 80", and page 21, line 22: 'Tween 20". Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants review the whole specification and make necessary changes to the trademarks wherever such recitations occur.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

9) Claims 41 and 43 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
  The amount of direction or guidance presented;

The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

Instant claims recite a protein having "at least 40%" similarity to a GroEL protein having an amino acid sequence of SEQ ID NO: 2. However, the instant specification is not enabled for such a protein having at least "at least 40%" similarity to the GroEL protein of SEQ ID NO:2, as claimed. One of ordinary skill in the art cannot envisage what sequences are encompassed in the claims, since the specification lacks algorithmic parameters used to determine percent identity. The recitations are not defined by the parametric values set when using an algorithm to compare sequences. Without a clear and unambiguous description of how to do the sequence comparison, the metes and bounds of the claims cannot be envisaged. Without a specific disclosure of an algorithm and values used in the algorithm, the sequence identity between two sequences has no common meaning within the art. Without such a disclosure of values used, one of ordinary skill in the art cannot be sure of the sequences embraced by the claims and would not be able to make and use those polypeptide sequences as recited in the instant claims without undue experimentation. The claims are viewed as not meeting the enablement provisions of 35 U.S.C § 112, first paragraph. Undue experimentation would have been required by one of ordinary skill in the art to reproducibly practice the invention as claimed due to the lack of specific guidance or disclosure of algorithmic values used to determine percent identity.

10) Claim 38-43 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Instant claims are drawn to a method for vaccinating an animal against infection by *L. intracellularis* or a related microorganism, or treating an animal infected by *L. intracellularis,* comprising administering to the animal an effective amount of a "derivative" of a 'peptide, polypeptide, or protein' from *L. intracellularis* or a related microorganism, which induces a

"protective immune response" against *L. intracellularis* or a related microorganism. However, the specification does not provide enablement for such a "derivative" of a 'peptide, polypeptide, protein' from *L. intracellularis* or a related microorganism, which induces a "protective immune response" against *L. intracellularis* or a related microorganism.

The instant claim is evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, the nature of the invention is related to a microbial peptide, polypeptide or protein and a 'derivative' thereof, for use as a vaccine composition in a method of inducing a "protective immune response". The breadth of the claims encompasses a "protective" "derivative"of an immunogenic peptide, protein or polypeptide of *L. intracellularis* or a related microorganism. However, the 'derivatives' of such an immunogenic peptide, protein or polypeptide of *L. intracellularis* or a related microorganism is not defined or enabled as a 'protective' immunogen against infections caused by *L. intracellularis* or a related microorganism. There is no disclosure or specific guidance within the instant specification teaching how to make such a 'derivative' such that it induces a 'protective' immune response against infections by *L. intracellularis* or a related microorganism.

Although a microbial peptide, polypeptide or protein of adequate size is expected in the art to generally induce an immune response, and some times a 'protective' immune response, the ability of a peptide, polypeptide or protein "derivative" to have similar immunogenic and protective properties is not always certain and often has to be established by evaluation and experimentation. There is no evidence in the instant specification showing that the claimed

peptide, polypeptide or protein 'derivative', does indeed induce a 'protective' immune response against infections by *L. intracellularis* or a related microorganism. The specification does not teach how a peptide, polypeptide or protein 'derivative' is produced, and whether or not it is made by varying specific amino acid residues of the claimed peptide, polypeptide or protein. If the latter is the case, the specification provides no guidance as to which specific amino acids may be varied without causing any detrimental effect to the claimed peptide, protein or polypeptide that is meant for use as a vaccine. There is no information in the instant specification with regard to which variations, i.e., insertions, deletions, additions and substitutions, of which amino acids in the claimed peptide, polypeptide or protein would result in a "derivative" that would retain the functional integrity or biological/immunogenic and protective competence of the native peptide, polypeptide or protein, without rendering it non-functional. This is important because the art reflects unpredictability as to which amino acids in a specific peptide, polypeptide or protein can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific peptide, polypeptide or protein. While it is known in the art that variation in one or more amino acids is possible in a given protein, polypeptide or peptide, the exact position within its amino acid sequence where replacements or variations can be made, with a reasonable expectation of success of retaining the peptide's, polypeptide's or protein's functional or immunogenic integrity, is not certain. A random replacement affecting the epitopic amino acid positions that are critical, for example, to the three-dimensional conformational structure and immunogenic property of the peptide, polypeptide or protein, would result in a product that may be non-functional (i.e., non-immunogenic) or not optimally immunogenic as a vaccine composition, because such positions tolerate no or little modifications. For instance, Houghten *et al.* (New Approaches to Immunization, *Vaccines86*, Cold Spring Harbor Laboratory, p. 21-25, 1986) teach the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten *et al.* state (see page 24):

> One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the

polyclonal pool.

Thus, the art reflects that variations in critical residues at specific positions in an amino acid sequence could result in a peptide which may induce an antibody that may not recognize or bind to the native microbial polypeptide. In the instant case, this is important because one of the purposes of the instant invention is to produce a peptide, polypeptide or protein 'derivative' in its biologically active and/or immunogenic form for use as a vaccine. The instant disclosure lacks guidance on the precise nature and extent of amino acid replacements or variations that can be made in the claimed peptide, polypeptide or protein in order to produce a "derivative" and lacks teaching with regard to which specific amino acid variations in what positions would result in an effective or optimally immunogenic vaccine product. Clearly, Applicants have provided no specific guidance to enable one of ordinary skill in the art to reproducibly practice the claimed invention without undue experimentation. Given the lack of guidance in the specification and the art-recognized unpredictability in determining amino acid variations that are acceptable, one of ordinary skill in the art could not make or use the claimed 'protective' 'derivative' without undue experimentation. One of ordinary skill in the art would not be able to make such a 'derivative' having the claimed function and use it, for example, as a vaccine, because there is no information as to what specific amino acid residues are embraced by the "derivative" of the claims. The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

11) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

12) Claims 1, 6-10, 12, 32, 37-41, 43, 94, 95, 108 and 109 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 1, 6, 7, 32, 37, 38 and 41 are vague and indefinite in the recitation:

"related microorganism", because it is unclear what is encompassed in this phrase. It is not clear what characteristics or properties a microorganism should have in order to qualify as a 'related microorganism'.

(b) Claim 40 is vague and indefinite in the recitation: "derivative thereof", because it is unclear what is encompassed in this recitation. It is not clear what characteristics a heat shock protein or a flagellar basal body rod protein should have in order to qualify as a "derivative thereof".

(c) In claim 41, it is unclear which protein of claim 40 provides antecedence for the recitation: "the protein is GroEL" (see line 1), because claim 41 depends from claim 40, which recites more than one protein. Clarification/correction is requested.

(d) Claims 9 and 40 are vague and indefinite in the recitation "refolding/heat shock protein", because it is unclear what "/" stands for. Does the / mean that 'refolding' is synonymous with 'heat shock'? Clarification/correction is requested.

(e) Claims 9 and 40 are vague and indefinite in the recitation: 'S-adenosylmethionine: tRNA ribosyltransferase-isomerase'. Does this phrase represent a single immunogenic component or a mixture of two immunogenic components? Clarification/correction is requested.

(f) In claims 37, 38 and 39, Applicants use the recitations: 'peptide', 'polypeptide' and 'protein'. It is unclear what the differences are between these recitations with respect to their meaning or scope.

(g) Claims 10 and 94 are vague and confusing in the recitation "immunologically" effective amount of a polypeptide (see line 2). The claim is drawn to a vaccine composition meant to be immunogenic. It is unclear what Applicants mean by an "immunologically" effective amount of a polypeptide. Is it equivalent to "immunogenically" effective amount?

(h) Claim 109 lacks antecedent basis for the recitation: "The method of claim 12". Claim 109 depends from claim 12. Claim 12 is drawn to a vaccine composition, but not to a method.

(i) Claims 94 and 95 are vague and indefinite in the recitation "under hybridization conditions", because it is unclear what is encompassed in this recitation. It is not clear whether the recitation encompasses high, low or medium stringency temperature conditions.

(j) Claim 95 is vague, confusing and/or redundant in the recitation: "a polypeptide comprising the sequence of a polypeptide comprising the sequence ..... and comprises an amino acid sequence".

(k) Claims 2, 6-9, 12, 43, 108 and 109, which depend directly or indirectly from claim 1, are also rejected under 35 U.S.C. § 112, second paragraph, because of the vagueness or indefiniteness in the base claim(s) identified above.

Rejection(s) under 35 U.S.C. § 102

13) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** The invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

14) Claims 1, 2, 6, 7, 32, 37 and 38 are rejected under 35 U.S.C. § 102(e) as being anticipated by Knittel *et al.* (US 5,714,375) as evidenced by Lemarchand *et al.* (*Vet. Pathol.* 34: 152-156, March 1997, abstract).

Knittel *et al.* disclose vaccines comprising an attenuated or avirulent immunogenic strain or antigen of *Ileal symbiont intracellualris* (i.e., *Lawsonia intracellualris*) contained in a pharmaceutically acceptable carrier. The antigen or vaccine is incorporated in a suitable adjuvant, such as, aluminum hydroxide or mineral oil (see abstract; column 6, paragraphs 4-7). A method of vaccinating pigs using the vaccine containing the immunogen (i.e., the recited immunogenic component) is taught. See column 7. That the prior art vaccine inherently comprises a *Lawsonia intracellualris* polypeptide or protein is inherent from the disclosure of

Knittel *et al.*, since attenuated whole cells of bacteria are known to contain polypeptides on their surface.

That the prior art *Ileal symbiont intracellualris* is synonymous with *Lawsonia intracellualris* is inherent from the teachings of Knittel *et al.* as evidenced by what is well known in the art. For instance, Lemarchand *et al.* teach that *Ileal symbiont intracellualris* is now known as *Lawsonia intracellualris* (see abstract).

The disclosure of Knittel *et al.* anticipates the instant claims. Lemarchand *et al.* is **not** used as a secondary reference in combination with Knittel *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Knittel *et al.* See *In re Samour* 197 USPQ 1 (CCPA 1978).

Claims 1, 2, 6, 7, 32, 37 and 38 are anticipated by Knittel *et al.*

15) Claims 1, 2, 6-9 and 94 are rejected under 35 U.S.C. § 102(b) as being anticipated by Labigne *et al.* (WO 94/26901 - Applicants' IDS).

It is noted that the paragraph bridging pages 3 and 4 of the instant specification recites as follows with regard to the limitation "related microorganism":

> ....Reference hereinafter to "*Lawsonia intracellularis*" or its abbreviation "*L. intracellularis*" includes all microorganisms similar to or otherwise related to this microorganism. For example, a **related microorganism** may have a nucleotide sequence similarity at the chromosome or extrachromosomal level of at least about 60%, more preferably at least about 70% and even more preferably greater than at least about 80% with respect to all or **part of** a nucleotide sequence within the chromosome or extrachromosomal elements of *L. intracellularis*. [Emphasis added].

Labigne *et al.* disclose a recombinant immunogenic composition of *Helicobacter felis* or *Helicobacter pylori*, i.e., a microorganism related to *Lawsonia intracellualris,* comprising at least a subunit urease polypeptide of at least one of the related microorganism and/or a Heat Shock Protein (HSP) (see abstract; claims and the paragraph bridging pages 36 and 37). A sequence search performed at the Office indicates 67.2% similarity between Applicants' polypeptide comprising SEQ ID NO: 2 and the prior art polypeptide (see enclosed search report). The immunogenic composition is present in a physiologically acceptable excipient or carrier and optionally in an adjuvant. The vaccine composition may be administered to humans as well as to

non-human animals for veterinary purposes (see page 11, lines 1-11). The proteinaceous material used in the immunogenic composition is comprised of peptides, polypeptides or proteins (see page 11, third full paragraph). The prior art HSP cross-reacts with GroEL-like proteins or GroES-like proteins from bacteria other than *Helicobacter* (see page 15, middle paragraph). That the prior art nucleotide sequence, which encodes a polypeptide showing 67.2% similarity with Applicants' polypeptide comprising SEQ ID NO: 2, hybridizes with Applicants' SEQ ID NO: 1 under the recited conditions is inherent from the teachings of Labigne *et al.*

Claims 1, 2, 6-9 and 94 are anticipated by Labigne *et al.*

Rejection(s) under 35 U.S.C. § 103

16) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

17) Claims 32, 37-41, 43, 94 and 95 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Labigne *et al.* (WO 94/26901 - Applicants' IDS).

The teachings of Labigne *et al.* are described above, which do not expressly teach a method of vaccinating an animal as recited in instant claims using their recombinant immunogenic composition. However, Labigne *et al.* specifically disclose that their vaccine composition may be administered to human as well as non-human animals for veterinary

purposes (see page 11). Since methods of vaccinating or treating an animal against a bacterial infection are well known in the art, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use Labigne's immunogenic vaccine composition in a method for vaccinating or treating an animal against infection(s) by a microorganism related to *L. intracellularis*, to produce the instant invention, with a reasonable expectation of success. One skilled in the art would have been motivated to produce the instant invention for the expected benefit of immunizing or treating an animal against infection(s) by a microorganism related to *L. intracellularis,* since Labigne *et al.* explicitly teach that their vaccine composition can be administered to human as well as non-human animals.

Claims 32, 37-41, 43, 94 and 95 are *prima facie* obvious over the prior art of record.

18) Claims 1, 2, 6-8, 32 and 37-39 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Joens *et al.* (US 5,610,059).

The reference of Joens *et al.* is applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C § 102 and accordingly is not disqualified under U.S.C 103(a).

Joens *et al.* disclose a composition comprising a purified PPE-causing agent (see abstract and claims). Joens *et al.* teach that this PPE-agent may be used to develop a whole organism bacterin or subunit preparation effective to prevent PPE. Joens *et al.* teach that the genetic material from the PPE-agent may be isolated and various useful fusion proteins may be prepared (see abstract). The PPE-agent is useful for developing prophylactic treatments including vaccines against PPE (see column 2, lines 48-51). Joens' disclosure is directed to the purification of the PPE-causing agent directed to uses in developing vaccines useful to eradicate PPE from the domesticated pig population (see column 2, lines 58-61; claims and Example 1). Joens *et al.* teach that because the PPE-causing agent may be cultured and purified, it is now possible to develop a bacterin (i.e., an inactivated PPE-causing agent, which is biologically inactive, yet antigenically intact), or inactivated preparation of the PPE-causing agent, using techniques known to the art, which may be administered to pigs as to permit the pigs to mount an effective immune response against the PPE-causing agent that fall within the scope of the

invention. See paragraph bridging columns 3 and 4. It is implicit that an inactivated preparation of the PPE-causing agent further contains a polypeptide macromolecule on its surface. Alternatively, various antigenic subunit preparations incorporating proteins from the PPE-causing agent could be prophylactically administered to pigs, which could an immune response against the PPE-causing agent. Using a classical biochemical approach, purified cell-surface proteins could be prepared from lysates of host cells infected with the PPE-causing agent. See column 4, first full paragraph. It is taught that using a purified preparation of the PPE-causing agent and recombinant DNA techniques, subunit vaccines against the PPE-causing agent can be developed. Genes that encode proteins related to known proteins, or that encode proteins likely to be antigenic in the PPE-causing agent, may be localized and subcloned into fusion-protein expression vectors. Such vectors may be expressed in heterologous bacterial, animal or plant cell hosts, or expressed in cell-free enzymatic transcription/translation systems. Antigenic fusion proteins encoded by such vectors may be purified and used as prophylactic immunogens in piglets. See paragraph bridging columns 4 and 5.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use Joens' purified PPE-causing agent to produce an inactivated bacterin as an immunogenic vaccine composition in pigs, or produce a recombinant subunit protein immunogen using the purified PPE-causing agent and the art known recombinant techniques for use in vaccination of pigs against infection by the PPE-causing agent, to produce the vaccine composition and the method of vaccination of the instant invention, with a reasonable expectation of success, because Joens *et al.* explicitly teach that their purified PPE-causing agent can be used to produce such a vaccine composition and such a method of vaccinating pigs. One skilled in the art would have been motivated to produce the instant invention for the expected benefit of producing a safe and effective vaccine composition and a method for vaccinating pigs against Porcine Proliferative Enteritis or PPE.

It is noted that the instant specification in the paragraph bridging pages 1 and 2 and on page 2 describes Porcine Proliferative Enteritis (PPE) to be the same as infections caused by *L.*

intracellularis. It is noted that Applicants' *L. intracellularis* is the same as Joens' PPE-causing agent. Claims 1, 2, 6-8, 32 and 37-39 are *prima facie* obvious over the prior art of record.

Objection(s)

19) Claims 1, 2, 6-10, 12, 32, 37-41, 43, 94, 95, 108 and 109 are objected to for the following reasons:

(a) Instant claims are objected to for including non-elected subject matter.

(b) Claims 12, 94 and 95 are objected to for lacking a preceding article before the recitation "nucleic acid". It is suggested that Applicants replace the recitation with --a nucleic acid--.

(c) Claim 108 is objected to for lacking a period at the end of the claim.

Remarks

20) Claims 1, 2, 6-10, 12, 32, 37-41, 43, 94, 95, 108 and 109 stand rejected. The polypeptide comprising the amino acid sequence of SEQ ID NO: 2 encompassed in claims 10, 12 and 108 is free of prior art currently of record.

21) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week.

22) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's

supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SD

S. Devi, Ph.D.
Primary Examiner
August 2001

XX
DE L. pneumophila HtpB gene product.
XX
KW Urease; immunogen; vaccine; diagnostic; heat shock protein; HSP;
KW GroEL-like protein; Helicobacter felis.
XX
OS Legionella pneumophila.
XX
PN WO9426901-A.
XX
PD 24-NOV-1994.
XX
PF 19-MAY-1994; 94WO-EP01625.
XX
PR 19-MAY-1993; 93EP-0401309.
PR 19-NOV-1993; 93WO-EP03259.
XX
PA (INRM) INST NAT SANTE & RECH MEDICALE.
PA (INSP) INST PASTEUR.
XX
PI Ferrero R, Labigne A, Suerbaum S, Thiberge J;
XX
DR WPI; 1995-006797/01.
XX
PT DNA from Helicobacter pylori and Helicobacter felis - used to
PT develop prods. for detection, treatment and prevention of
PT Helicobacter infection
XX
PS Disclosure; Fig. 7A(i-vii); 168pp; English.
XX
CC The sequence of the Helicobacter pylori heat shock protein A
CC (given in AAR67374) was compared to that of other GroEL-like
CC proteins from Legionella pneumophila (AAR67381), Escherichia coli
CC (AAR67382), Chlamydia psittaci (AAR67383), Mycobacterium leprae
CC (AAR67384) and human mitochondrial protein P1 (AAR67385), and regions
CC of homology were identified.
XX
SQ Sequence 547 AA;

Query Match 67.2%; Score 1820.5; DB 16; Length 547;
Best Local Similarity 66.6%; Pred. No. 3.8e-112;
Matches 363; Conservative 82; Mismatches 97; Indels 3; Gaps 2;

```
Qy       3 SKEILFDAKAREKLSRGVDKLANAVKVTLGPKGRNVVIEKSFGSPVITKDGVSVAKEIEL 62
           :||: |   || ::  ||: ||:||:||:||:|||||:|||:|:| :||||||||||||
Db       2 akelrfgddarlqmlagvnaladavqvtmgprgrnvvleksygaptvtkdgvsvakelef 61

Qy      63 EDKFENMGAQMVKEVAPKTSDIAGDGTTTATVLAQAIYREGVKLVAAGRNPMAIKRGIDK 122
           | :| |||||||||||| |||| ||||||||||||::|  || | |||| ||| :||||||
Db      62 ehrfmnmgaqmvkevasktsdtagdgtttatvlarsilveghkavaagmnpmdlkrgidk 121

Qy     123 AVVAVTKELSDITKPTRDQKEIAQVGTISANSDTTIGNIIAEAMAKVGKGGVITVEEAKG 182
           ||:|||||:|  ::|| :| | ||||||||||||  || |||||| |||| ||||||:  |
Db     122 avlavtkklqamskpckdskaiaqvgtisansdeaigaiiaeamekvgkegvitvedgng 181

Qy     183 LETTLDVVEGMKFDRGYLSPYFVTNPEKMVCELDNPYILCNEKKITSMKDMLPILEQVAK 242
           ||  | |||||:|||||:||||: | : | |||::|:||  :||::|:::|| :|| |||
Db     182 lenelyvvegmqfdrgyispyfinnqqnmscelehpfillvdkkvssiremlsvlegvak 241

Qy     243 VNRPLLIIAEDVEGEALATLVVNKLRGALQVVAVKAPGFGERRKAMLEDIAILTGGEAIF 302
             |||||||||:|||||||||||| :|| ::| ||||||||:||||||:|||||| |: |
Db     242 sgrplliiaediegealatlvvnnmrgivkvcavkapgfgdrrkamlqdiailtkgqvis 301

Qy     303 EDRGIKLENVSLSSLGTAKRVVIDKENTTIVDGAGKSEDIKARVKQIRAQIEETSSDYDR 362
           |: |  ||  :|  ||:|||:::  | |||:|| ||: :| ||: |||||:|||:||||||
Db     302 eeigkslegatledlgsakriivtde-ttiidgegkateinariaqiraqmeettsdydr 360

Qy     363 EKLQERLAKLVGGVAVIHVGAATETEMKEKKDRVEDALNATRAAVEEGIVPGGGTAFVRS 422
           ||||||:||| |||||| |||||| |||||| ||||||:|||||||||||| ||| | :|:
Db     361 eklqervaklaggvavikvgaatevemkekkarvedalhatraaveegivagggvalira 420

Qy     423 IKVLDDIKPADDDELAGLNIIRRSLEEPLRQIAANAGYEGSIVVEKVREPKDGFGFNAAS 482
           | || :|  :||:  |:||:||::| |:|||  ||||| |:|| || | || :||||||:
Db     421 qkaldslkgdnddqnmginilrraiespmrqivtnagyeasvvvnkvaehkdnygfnaat 480

Qy     483 GEYEDLIKAGVIDPKKVTRIALQNAASVASLLLTTECAIAEKPEPKKDMPMPGGGMGGMG 542
           ||| |::: |::|| ||||:|||||||||||:||||| :|:   |||:  :  | |||||
Db     481 geygdmvemgildptkvtrmalqnaasvaslmlttecmvadl--pkkeegvgagdmggmg 538

Qy     543 GMDGM 547
           || ||
Db     539 gmggm 543
```